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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
07/402,450	09/01/1989	GEORGE J. MURAKAWA	2124-154	8131

6449 7590 06/06/2007

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
06/06/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	07/402,450	MURAKAWA ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *114-151 and 190-248* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *114-151 and 190-248* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Prosecution Application

1. This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 41.37.

This submission complies with the requirements.

Status

2. Claims 114-151 and 190-248 are pending.

Claims 114-151 and 190-248 are rejected.

Any rejection which is not reiterated in this action is withdrawn as no longer applicable.

Claim Analysis

3. The claims were amended to require that the reference RNA and target RNA sequences are of similar length and amplified by the same primers. These amended claims must be analyzed in light of the decision of the Board of Patent Appeals and Interferences in Interference 105,055 between Wang and the current Murakawa application. The BPAI found that the Murakawa claim at issue, claim 50, was

anticipated/obvious by the Wang claims except for one element, as the BPAI notes at page 21 of paper 47 (April 5, 2004),

> **In view of this record, including the testimony of Dr. Joyce cited above, we find that proposed Murakawa claim 50 would not have immediately suggested using a reference sequence which binds to the same primers as the target sequence in the same PCR amplification reaction mixture. The definition of a reference sequence distinguishable from a target sequence by size is broad and general and does not particularly suggest a reference sequence which binds to the same primer pair as a target sequence.**

The BPAI provides that the express difference between the Wang and Murakawa claims is that Wang required the use of primers that can amplify both the reference and target sequences and Murakawa did not. Therefore, the new claim amendment, which now requires the use of primers that can amplify both the reference and target sequences renders the claims unpatentable under 35 U.S.C. 135(b) and 35 U.S.C. 103 in view of Wang, since the claims are now prior art relative to one another.

Applicant argues, at page 37 of the response, that Wang is not prior art. However, Applicant incorrectly analyzes the BPAI decision. Applicant appears to argue that the decision doesn't mean what it says, since the claim 50 at issue of Murakawa never included the limitation argued by Applicant. In fact, Wang is properly prior art under 35 U.S.C. 135(b) and will be applied below.

Claim Rejections - 35 USC § 135(b)

4. The following is a quotation of 35 U.S.C. 135(b)(1) which forms the basis for all the rejections set forth in this Office action:

> (b)(1) A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted.

5. Claims 114, 115, 117, 118, 120, 122, 123, 125, 126, 128, 130, 131, 133, 134, 136, 138, 141, 142, 144, 146-151, 190-192, 194, 195, 197, 199-201, 203, 204, 206, 208-210, 212, 213, 215, 217-219, 221, 222, 224 and 226-248 are rejected under 35 U.S.C. 135(b)(1) as not being made prior to one year from the date on which U.S. Patent No. 5,219,727 was granted. See *In re McGrew*, 120 F.3d 1236, 1238, 43 USPQ2d 1632, 1635 (Fed. Cir. 1997) where the Court held that 35 U.S.C. 135(b) may be used as a basis for *ex parte* rejections.

Wang teaches a method of claims 114, 122, 130, 138, 146, 190, 199, 208, 217, 226, *a process for quantitation of a target viral RNA in a sample which comprises* (see claim 1, "method for quantifying a target nucleic acid segment in a sample" and claim 8, where the sequence may be from HIV, which is an RNA virus),

(i) selecting a sequence present in the target viral RNA; (see claim 1, "(a) adding to said sample a predetermined initial amount of standard nucleic acid segment wherein said standard nucleic acid segment binds to same primers as are bound by said target nucleic acid segment in a reaction mixture", where a target nucleic acid sequence is selected),

(ii) adding a known quantity of a reference RNA sequence to the sample, wherein the reference RNA sequence consists of the selected target viral RNA sequence with a

multibase insert into a site within the selected target viral RNA sequence, wherein the reference RNA sequence and the selected target viral RNA sequence are of similar length and can be amplified and detected by the same oligonucleotides and wherein following amplification amplified reference RNA sequence and amplified selected target viral RNA sequence are distinguishable by size or by probe (see claim 1, "(a) adding to said sample a predetermined initial amount of standard nucleic acid segment wherein said standard nucleic acid segment binds to same primers as are bound by said target nucleic acid segment in a reaction mixture", where a target nucleic acid sequence is selected", and step b of claim 1, "(b) treating said sample under conditions suitable for carrying out a polymerase chain reaction, wherein said nucleic acids are rendered single-stranded and exposed to an agent for polymerization, deoxynucleoside 5' triphosphates, and a pair of oligonucleotide primers, wherein said pair of primers is specific for both the target and standard nucleic acid segments, such that an extension product of each primer of said pair can be synthesized using separate strands of the target and standard segments as a template for synthesis, such that the extension product of one primer, when it is separated
from the template strand, can serve as a template for the synthesis of the extension product of the other primer of said pair wherein said amplified target and standard segments are distinguishable by size or by the use of
internal probes, wherein said internal probes may be differentially labeled for each of said amplified target and standard segments; where Wang teaches references and Targets that are amplified by the same oligonucleotides and see claim 6, where the

target is within an mRNA sequence and see figures 2 and 3, where the size renders the target and reference distinguishable),

(iii) simultaneously subjecting the selected target viral RNA sequence and the reference RNA sequence in the sample to polymerase chain reaction amplification under conditions appropriate to simultaneously amplify the selected target viral RNA sequence if present in the sample and the reference RNA sequence (see step (b) of claim 1 of Wang, "(b) treating said sample under conditions suitable for carrying out a polymerase chain reaction, wherein said nucleic acids are rendered single-stranded and exposed to an agent for polymerization, deoxynucleoside 5' triphosphates, and a pair of oligonucleotide primers, wherein said pair of primers is specific for both the target and standard nucleic acid segments, such that an extension product of each primer of said pair can be synthesized using separate strands of the target and standard segments as a template for synthesis, such that the extension product of one primer, when it is separated from the template strand, can serve as a template for the synthesis of the extension product of the other primer of said pair wherein said amplified target and standard segments are distinguishable by size or by the use of internal probes, wherein said internal probes may be differentially labeled for each of said amplified target and standard segments;;

(iv) measuring the amounts of the amplified selected target viral RNA sequence and the amplified reference RNA sequence; (see step (e) of claim 1 of Wang, (e) measuring the amounts of the amplified target and standard segments produced in step (d));

(v) determining the amount of the target viral RNA present in the sample before amplification from the amount of the amplified selected target viral RNA sequence and the amount of the amplified reference RNA sequence (see claim1, step (f) of Wang, "calculating from the amplified target and standard segments produced in step (d) the amount of said target nucleic acid segment present in the sample before amplification.")

With regard to claims 115, 123, 131, 139, 147, 149, 192, 201, 210, 219, 228, Wang teaches the analysis of HIV (see claim 8, where HIV proteins are analyzed).

With regard to claim 117, 125, 133, 141, 194, 203, 212, 221, Wang teaches measurement of the amount of amplified target and reference RNA signals (see claim 6 of Wang, "The method of claim 4 wherein the pair of oligonucleotide primers of step (b) is labeled, and the amounts of amplified target and standard segments produced are measured according to step (e) by determining the amount of label incorporated into each of said amplified nucleic acid segments.")

With regard to claims 118, 120, 126, 128, 134, 136, 142, 144, 195, 197, 204, 206, 213, 215, 222, 224, Wang teaches the use of labeled probes and primers (see claim 6).

With regard to claim 148, Wang teaches a reverse transcription reaction (see claim 4) and teaches the other elements as discussed in the base rejection above.

With regard to claims 150-151, 229-234, the BPAI in the decision in Paper 36, expressly barred claims 46 and 47, which were drawn to the reaction mixtures identical to claims 150 and 151 by the Wang patent.

With regard to claims 191, 200, 209, 218, 227, Wang teaches internal sequences which include unrelated sequences (see claim 5, drawn to the AW108 plasmids which have unrelated sequences as shown in figure 1).

With regard to claims 235-248, Wang teaches the use of multiple multibase inserts, each of which is about 21 bases in length (see claim 5 and figure 1 and especially claim 10, where the inserts are each approximately 21 basepairs in length).

6. Claims 116, 119, 121, 124, 127, 129, 132, 135, 137, 139, 140, 143, 145, 193, 196, 198, 202, 205, 207, 211, 214, 220, 223 and 225 are rejected under 35 U.S.C. 135(b)(1) as not being made prior to one year from the date on which U.S. Patent No. 5,219,727 was granted in view of Mullis et al (U.S. Patent 4,683,195). See *In re McGrew*, 120 F.3d 1236, 1238, 43 USPQ2d 1632, 1635 (Fed. Cir. 1997) where the Court held that 35 U.S.C. 135(b) may be used as a basis for *ex parte* rejections.

Wang teaches the limitations of claims 114, 115, 117, 118, 120, 122, 123, 125, 126, 128, 130, 131, 133, 134, 136, 138, 141, 142, 144, 146-151, 190-192, 194, 195, 197, 199-201, 203, 204, 206, 208-210, 212, 213, 215, 217-219, 221, 222, 224 and 226-248 as discussed above.

Wang does not teach the use of T7 promoters on primers or radioisotopes.

Mullis teaches the use of T7 promoters (see colum 29, lines 40-50) as well as the use of radioisotopes (see column 25, line 34).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the T7 promoters and radioisotopes of Mullis in the invention of Wang in order to permit easier detection using the radiolabel and in order to

express more RNA when desired as taught by Mullis. As the Federal Circuit has noted in DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 80 USPQ2d 1641, 1651 (Fed. Cir. 2006),

> Indeed, we have repeatedly held that an implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the "improvement" is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal—and even common-sensical—we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan possesses knowledge and skills rendering him *capable* of combining the prior art references.

The current situation not only has specific motivation as noted, but there is clearly implicit motivation as discussed by Dystar.

Response to Arguments

7. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Applicant's sole argument that is applicable to the new rejections, necessitated by the amendment, is that Wang is not a proper 135(b) bar. However, as noted above, Wang is a proper 135(b) reference because the issue on which the board decided the

claims were substantially the same related to the precise amendment that Applicant has made in these claims. Therefore, the rejections is applied.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

5/31/05